

each j and e is 0 or 1, with the sum of j and e equal to 1.

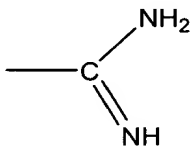
### REMARKS

Claims 2-5, 7-12, and 33 were pending. An amendment to claim 33 is presented. No new matter has been added. In view of the amendment and the remarks that follow, Applicants respectfully request that all rejections be withdrawn.

#### Rejections under 35 U.S.C. §112, second paragraph

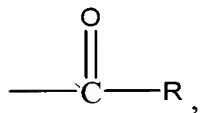
Claim 33 stands rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention. In particular, the Final Rejection alleges that the terms “keto”, “carboxyl” and “amidine” are confusing. The Advisory Action states that, at least the term “keto” remains unclear. As discussed below, Applicants believe all terms are clear. The proper inquiry, when determining whether a claim satisfies the requirements of 35 U.S.C. § 112, second paragraph, is a determination “whether those skilled in the art would understand what is claimed when the claim is reading light of the specification.” *Orthokinetics Inc. v. Safety Travel Charis, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986). Thus, if those skilled in the art can understand what is claimed when the claim is read in light of the specification, a rejection under 35 U.S.C. § 112, second paragraph, is inappropriate.

Applicants respectfully assert that one skilled in the art would understand the meaning of the terms and the scope of the claim containing the terms “keto”, “carboxyl”, and “amidine”. Amidine is a group of the structure:



where the “—” represents the site of binding for this group. It would be clear to one skilled in the art what is meant by such a group. Similarly, one skilled in the art would understand that a “carboxyl” moiety is of the formula  $\text{—CO}_2\text{H}$ . Finally, a “keto” group is

a ketone moiety (see, for example, McGraw-Hill Dictionary of Scientific and Technical Terms, 5<sup>th</sup> Ed., 1994). In the instant context, the ketone group is of the formula:



where R is alkyl, aryl or heterocycle (*Id.*). The scope of structure encompassed by alkyl, aryl, and heterocycle groups is well known to one skilled in the art. Further, these terms are discussed in detail in the instant application (see, for example, page 15, line 5 to page 17, line 26 of the filed specification). Thus, one skilled in the art would understand the scope of structures containing the moieties cited in the rejection. As the scope of claims comprising the disputed terms would be understood by one skilled in the art, Applicants respectfully request reconsideration and withdrawal of the rejection.

#### **Rejections under 35 U.S.C. § 103**

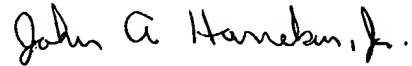
Claims 2-5, 7-12, and 33 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gordeev et al. (WO 96/33972), Grandoni (U.S. 5,998,420) and Hamprecht et al. (U.S. 5,591,694) in view of Gordon et al. (J. Med. Chem. 37, pp. 1385-1401, 1994). Applicants note that all allegations presented by the Office Action concern compound I of claim 33. While Applicants disagree with the allegations of the Office Action, the proposed amendment removes compound I from claim 33 in order to further prosecution. As such, Applicants believe that the rejection is moot and request that the rejection be withdrawn.

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8366 if there are any questions regarding Applicants' claimed invention.

**Docket No.: ISIS-2202**

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned This attachment is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

A handwritten signature in black ink that reads "John A. Harrelson, Jr." The signature is written in a cursive, slightly slanted style.

John A. Harrelson, Jr.  
Registration No. 42,637

Date: April 10, 2003

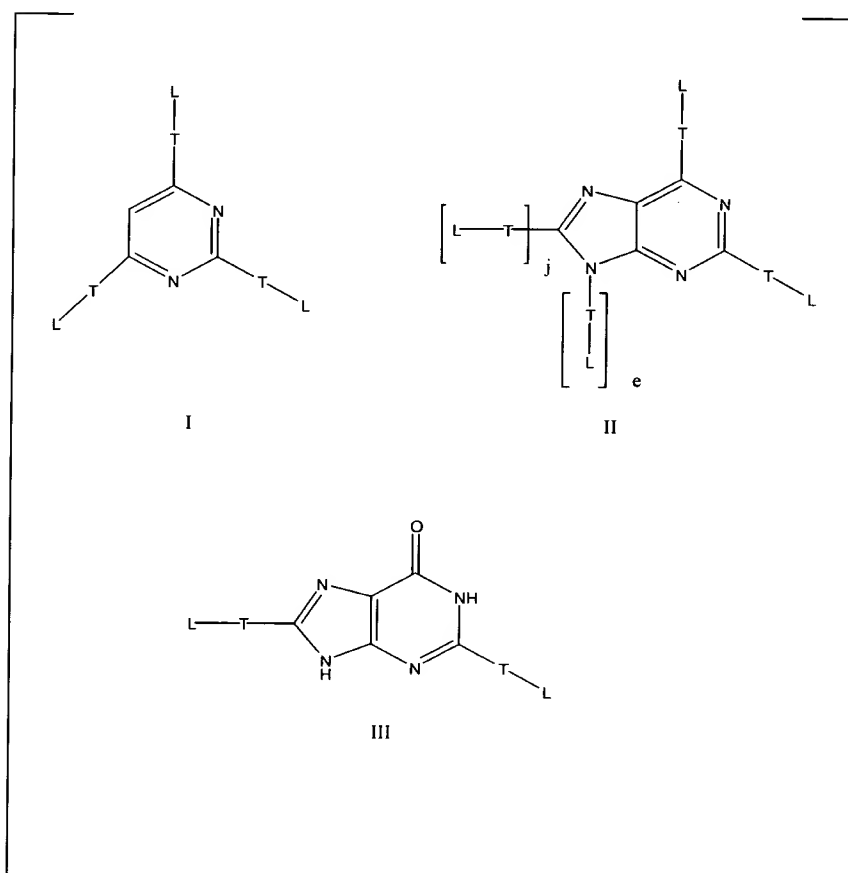
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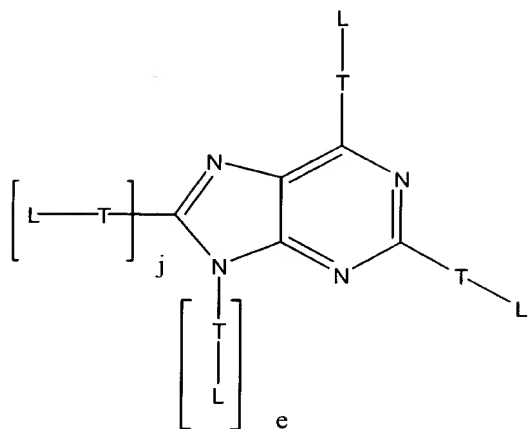
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

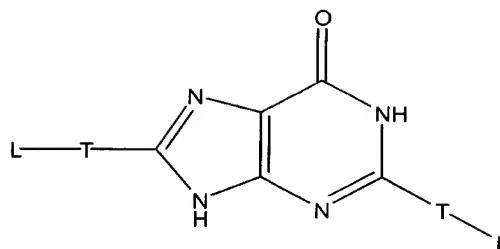
Please amend claim 33 as follows.

33. A mixture comprising a set of at least six chemical compounds having a common heterocyclic scaffold bearing functionalizable atoms, wherein said set of compounds is represented by one of structures [I,] II or III:





II



III

[wherein for structure I:

each tether moiety T is -NH(R<sup>1</sup>)NH-, -NH(R<sup>1</sup>)O-, -NHR<sup>2</sup>NH-, -NHR<sup>2</sup>SO<sub>2</sub>NH-, -NHR<sup>1</sup>-, -N(R<sup>4</sup>)<sub>2</sub>, -N=N-, O, S, Se, -P(=O)(O)<sub>2</sub>, NH, OR<sup>2</sup>, OR<sup>3</sup>, malonato, pyrrolidinyl, piperidinyl, piperidinylmethylene, piperazinyl, or morpholino;

R<sup>1</sup> is alkylene; R<sup>2</sup> is aryl; R<sup>3</sup> is H or C<sub>1</sub>-C<sub>10</sub> alkyl; R<sup>4</sup> is alkylenoxy; and

each chemical substituent L is, independently, C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, substituted C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>4</sub>-C<sub>7</sub> carbocyclic alkyl, substituted C<sub>4</sub>-C<sub>7</sub> carbocyclic alkyl, C<sub>4</sub>-C<sub>10</sub> alkenyl carbocyclic, substituted C<sub>4</sub>-C<sub>10</sub> alkenyl carbocyclic, C<sub>4</sub>-C<sub>10</sub> alkynyl carbocyclic, substituted C<sub>4</sub>-C<sub>10</sub> alkynyl carbocyclic, a nitrogen, oxygen or sulfur containing saturated heterocycle, a substituted nitrogen, oxygen or sulfur containing saturated heterocycle, a benzo-fused heterocycle, a substituted benzo-fused heterocycle, a substituted or unsubstituted saturated mixed heterocycle; wherein each of the substituent groups is selected from a group consisting of alkyl, alkenyl, alkynyl, aryl, hydroxyl, alkoxy, benzyl, nitro, thiol, thioalkyl, thioalkoxy and halo; or L is, independently, piperazine, pyridazine, pyrazine, triazine, phthalimido, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR<sup>1</sup>R<sup>2</sup>, CONR<sup>1</sup>, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido,

hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, or a carbohydrate;

and for structures II and III:]

each tether moiety T is -NH(R<sup>1</sup>)NH-, -NH(R<sup>1</sup>)O-, -NHR<sup>2</sup>NH-, -NHR<sup>2</sup>SO<sub>2</sub>NH-, -NHR<sup>1</sup>-, -N(R<sup>4</sup>)<sub>2</sub>, -N=N-, O, S, Se, -P(=O)(O)<sub>2</sub>, NH, OR<sup>2</sup>, OR<sup>3</sup>, malonato, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, imidazolyl, pyrrolyl, pyrazolyl, indolyl, 1H-indolyl,  $\alpha$ -carbolinyl, carbazolyl, phenothiazinyl, phenoxazinyl, tetrazolyl, or triazolyl;

R<sup>1</sup> is alkylene; R<sup>2</sup> is aryl; R<sup>3</sup> is H or C<sub>1</sub>-C<sub>10</sub> alkyl; R<sup>4</sup> is alkyleneoxy; and

each chemical substituent L is, independently, C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, substituted C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>4</sub>-C<sub>7</sub> carbocyclic alkyl, substituted C<sub>4</sub>-C<sub>7</sub> carbocyclic alkyl, C<sub>4</sub>-C<sub>10</sub> alkenyl carbocyclic, substituted C<sub>4</sub>-C<sub>10</sub> alkenyl carbocyclic, C<sub>4</sub>-C<sub>10</sub> alkynyl carbocyclic, substituted C<sub>4</sub>-C<sub>10</sub> alkynyl carbocyclic, C<sub>6</sub>-C<sub>14</sub> aryl, substituted C<sub>6</sub>-C<sub>14</sub> aryl, heteroaryl, substituted heteroaryl, a nitrogen, oxygen or sulfur containing heterocycle, a substituted nitrogen, oxygen or sulfur containing heterocycle, a mixed heterocycle, or a substituted mixed heterocycle; wherein each of the substituent groups is selected from a group consisting of alkyl, alkenyl, alkynyl, aryl, hydroxyl, alkoxy, benzyl, nitro, thiol, thioalkyl, thioalkoxy and halo; or L is, independently, phthalimido, an ether having 2 to 10 carbon atoms and 1 to 4 oxygen or sulfur atoms, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR<sup>1</sup>R<sup>2</sup>, CONR<sup>1</sup>, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, or a carbohydrate; and

each j and e is 0 or 1, with the sum of J and e equal to 1.